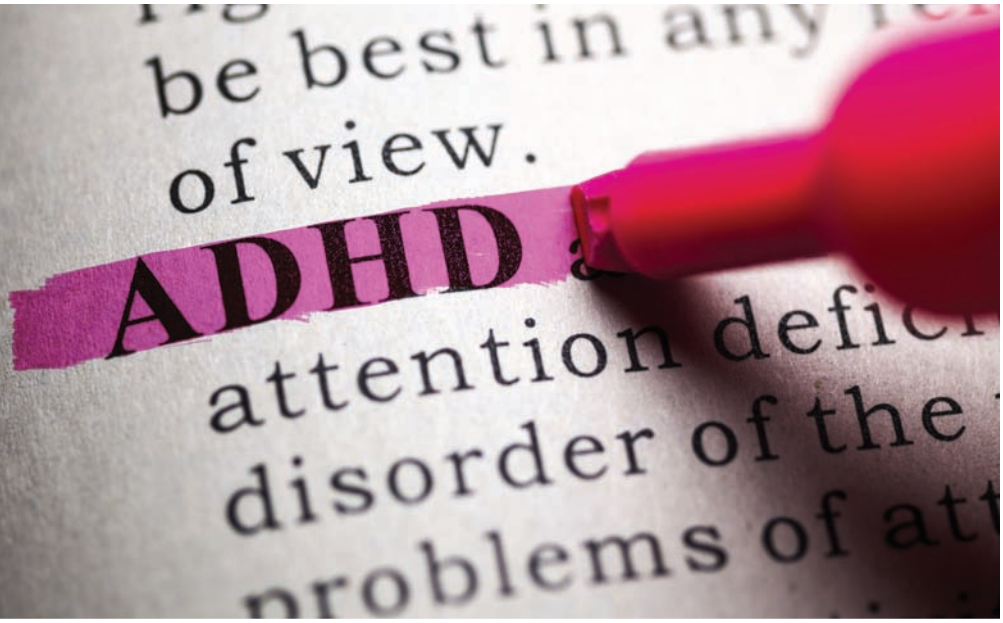

OUR CURRENT UNDERSTANDING OF ADULT ADHD

by Steven D. Targum and Lenard A. Adler

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INTRODUCTION

Dr. Targum: There is an increasing awareness that attention deficit hyperactivity disorder (ADHD) is present in adults and that the symptoms and functional consequences of the disorder have been ongoing since childhood.[1–6] The core symptoms of ADHD include inattention, distractibility, hyperactivity, and impulsivity.[2] Although the hyperactivity symptoms may abate in some ADHD adults, the inattention and distractibility symptoms often persist and contribute to interpersonal, social, family, academic, and work-related difficulties.[4–6]

In contrast to children and adolescents, adult ADHD has been less diagnosed and is often mis-diagnosed, under-treated when recognized, or not treated at all.[7] Consequently, I thought it would be important to explore the topic of adult ADHD with an expert.

I spoke with Lenard A. Adler, MD, Professor of Psychiatry and Child and Adolescent Psychiatry at New York University School of Medicine and Director of the adult ADHD program at New York University Medical Center in New York City. We discussed his research and perspective on the current status of adult ADHD assessment and treatment.

Dr. Adler, can you describe ADHD?

Dr. Adler: There are three different presentations of ADHD that are differentiated by the most dominant presenting symptoms.[2,7–9] First, the *predominantly inattentive presentation* describes an ADHD patient who is easily distracted and cannot get organized or finish a task, is not attentive to details, cannot follow instructions or conversations, and may seem careless or sloppy. Most adults with ADHD describe attention difficulties and admit that they often forget to complete the details of their daily routines. Secondly, there is the *predominantly hyperactive-impulsive presentation* who fidgets and talks a lot, cannot sit still for long and seems to be constantly moving or restless. The hyperactive ADHD patient is often impatient, has trouble with impulsivity, may blurt out comments or interrupt conversations, may get into trouble by not thinking before acting, and may get into more accidents or injuries. Finally, there may be a *combined presentation* in which the symptoms of both types of ADHD are present.

How common is ADHD?

Dr. Adler: ADHD is very common. ADHD affects 6 to 9 percent of children, and clinically significant symptoms persist into adulthood in 60 percent of cases. Often, the diagnosis is not made until a person reaches adulthood.[10,11] Epidemiologic data indicate that the prevalence of ADHD in adults is approximately four percent worldwide. In the United States, about eight million adults have ADHD, making it one of the

most common psychiatric disorders. Boys are four times greater risk than girls.[10,11]

How is the diagnosis of ADHD made?

Dr. Adler: In children, the clinician can usually identify a pattern of behavioral problems and school difficulties that result from problems with inattention and/or hyperactivity. As part of the differential diagnosis of ADHD, other conditions need to be ruled out. In children, these disorders, including learning disabilities, oppositional defiant disorder, bipolar and depressive disorders, conduct disorder, anxiety disorder, and Tourette's syndrome can produce symptoms similar to ADHD.[7–9]

In adults, the ADHD symptoms must have begun in childhood and continued into adulthood. The recently adopted *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) criteria require that adults must have had multidensional ADHD symptoms before the age of 12.[2] Clinicians need to assess ADHD symptoms that have been present in the past six months as well as symptoms that occurred since childhood. There is often a history of childhood behavioral or school difficulties that, in retrospect, may be consistent with undiagnosed ADHD.

Clinicians should screen a patient for ADHD who presents with a history of concentration difficulties or poor organization and planning. Some other symptoms that may warrant screening for ADHD are complaints of poor memory, forgetfulness, trouble mood lability, low self-esteem, and poor self-discipline.

There are four key features that must be identified in order to meet the DSM-5 diagnostic criteria for adult ADHD:[2]

1. Identification of an early childhood onset that might have been undiagnosed ADHD
2. Documentation of at least five current, significant symptoms of either inattention or hyperactivity/impulsivity
3. Significant behavioral or functional impairment in at least two settings (home, work, school, social) that have resulted from the ADHD symptoms (evidence of impact)
4. Symptoms that are best explained by ADHD and not by another psychiatric disorder

In addition, there are some specific rating scales that can be used to determine if an individual meets the diagnostic criteria for ADHD.

What rating scales can be used to assess ADHD?

Dr. Adler: Several instruments have been developed to assess the diagnosis and symptoms of ADHD in adults. I'll just briefly mention two diagnostic and three symptomatic scales.

For diagnostic assessment, the Conners Adult ADHD Diagnostic Interview for DSM-IV (CAADID) is a semi-structured interview that assesses ADHD in adults based on the criteria of the fourth edition of the DSM (DSM-IV).[12] A second diagnostic instrument is the Adult ADHD Clinician Diagnostic Scale version 1.2 (ACDS v1.2).[3] The ACDS is a semi-structured clinician administered interview that begins with a retrospective assessment of childhood ADHD symptoms followed by a prompted, adult-specific assessment of the 18 ADHD symptoms that have been present in the past six months. The ACDS v1.2 was validated in the National Comorbidity Survey and in a variety of treatment trials as well.[10,11,13,14]

For symptomatic assessment, the ADHD Rating Scale IV, Investigator Administered and Scored (ADHD-RS-IV), is a validated clinician-administered scale that is designed to assess current symptomatology.[14] There is also a patient self-rated version of this scale called the adult ADHD Self-Report Scale (ASRS).[15] The Adult ADHD Investigator Symptom Rating Scale (AISRS) is another clinician-administered scale that assesses each symptom domain of ADHD.[16] The AISRS stem questions are designed to better capture symptoms of the disorder as it presents in adulthood. The AISRS has been found to be a valid measure of medication response in adults with ADHD as well.

How often does ADHD continue into adulthood?

Dr. Adler: Research studies have suggested that 30 to 70 percent of children with ADHD continue to have symptoms of the disorder when they become adults.[10,11,17] Unfortunately, the diagnosis of adult ADHD is vastly under-recognized. Only 10 to 25 percent of adults with ADHD are actually diagnosed and adequately treated.[10,11] In one recent survey, it was found that despite seeing a healthcare professional in the past year, more than 40 percent of the patients who met the criteria for adult ADHD had not been diagnosed, and that only 10 percent of these adult ADHD patients had received any treatment for the disorder.[17]

Is adult ADHD the same condition or is it different from adolescent ADHD?

Dr. Adler: The symptoms are often the same in adolescents and adults but the impact of many years of persistent ADHD symptoms may have had profound consequences on both the personal and professional

lives of the adults.[4,5] Some of the intensity of the hyperactivity symptoms may decline in adults. Some studies have found that clinically significant levels of hyperactivity and impulsivity are still present in half of adult ADHD patients but that prominent inattention symptoms persist in up to 90 percent of these individuals.

What are the causes (etiology) of ADHD?

Dr. Adler: It is likely that ADHD results from multiple causes just as there are three different clinical presentations. One of many hypotheses is that ADHD is a hypoarousal disorder resulting from decreased tonic activity of the locus coeruleus norepinephrine system that taxes executive control mechanisms.[18,19]

Is there a genetic component to ADHD?

Dr. Adler: Yes. It has been shown that ADHD is highly heritable.[20] However, the genetic basis for ADHD is not clear and much of the genetic studies to date has been inconsistent or contradictory. Genome-wide linkage and association studies have not detected effects at significant thresholds. These genetic studies are further complicated by the likely existence of both rare and common genetic risk variants for ADHD and genotype-environment interactions. Perhaps the most progress has been made in the search for rare variants, where several groups have found insertions and deletions in the genome that appear to explain a small subset of ADHD cases.

Let's explore the association between ADHD and fatigue. How do you sort this out?

Dr. Adler: Many patients with ADHD do complain of fatigue symptoms as well.[21] In fact, some of the symptoms of ADHD like inattention and distractibility, failure to pay close attention to details, difficulty sustaining attention, and difficulty organizing tasks or activities do overlap with fatigue. However, I think that the fatigue symptoms in ADHD subjects may be more of a consequence of ADHD symptoms (such as hyperactivity) or related sleep disturbance (such as sleep deprivation) than a core part of the illness itself. Hyperactivity may be exhausting in itself. It's reasonable to assume that persistent efforts at cognitive (executive) control of attention may cause distractibility, mental lapses, and that attentional fatigue can lead to decreased motivation and less ability to perform basic tasks.

The medications we use to treat ADHD may also occasionally cause fatigue as a side effect.[21]

Some people have noted that psychostimulants might induce fatigue when their effects wear off. However, there are few published studies that identify symptoms of fatigue following administration of these medications in ADHD. In fact, fatigue is infrequently reported as an adverse event in the *Physician's Desk Reference* (PDR) 2012 prescribing information of commonly used psychostimulants: less than one percent of patients receiving methylphenidate HCL and 2 to 4 percent taking lisdexamfetamine or mixed amphetamine salts.[21] Of course, fatigue may follow the abrupt cessation of these medications after prolonged administration.

What about sleep disturbance and ADHD?

Dr. Adler: Sleep disturbance, particularly sleep deprivation has been associated with ADHD.[22–24] Clearly, cognitive performance can be adversely affected by sleepiness and sleeplessness.

In a study of 122 adolescents with ADHD and 105 non-ADHD controls, Mick et al[23] found that treatment with psychostimulants, as well as comorbidity with anxiety and behavior disorders, was significantly associated with sleep disturbances. However, children with ADHD have more sleep disturbances than controls whether they were receiving medication or not.

Surman et al[24] investigated sleep disturbance in 182 adults with ADHD and 117 non-ADHD controls using a 22-question self-report survey.[24] The adults with ADHD experienced daytime sleepiness and reported more sleep problems than controls. Sleep impairment was significantly associated with ADHD. The mean number of sleep problems reported by the ADHD group was significantly greater than the controls ($p<0.001$) while controlling for ADHD pharmacotherapy, co-morbidities, or the age of ADHD onset.

How are adults with ADHD treated? Is it different than adolescents?

Dr. Adler: Education, pharmacotherapy and psychotherapy are all used in the treatment of ADHD patients regardless of their age.[7,13,14,25] Psychosocial treatments can be helpful for adults with ADHD, but medications are often prescribed as well. Medications are more commonly prescribed for adults as compared to children, in part because adults have lived with their symptoms through all of their lives. There are four approved sustained release stimulants and one approved non-stimulant: Strattera (atomoxetine HCl). The immediate release stimulants are also used, but they are "off label" for adults.

A key consideration in adults is the use of other medications that

might interact with stimulants, the potential for substance abuse, and other medical conditions that may complicate treatment.

What are the current pharmacologic treatment strategies for adults with ADHD?

Dr. Adler: Stimulant drugs like methylphenidate and dextroamphetamine have been used to treat ADHD for over 30 years.[1,7,25] These medications come as pills, patches, and chewable tablets. The daily dosage of these stimulant drugs is often divided into two or three times per day. Consequently, many clinicians prescribe longer acting or extended release stimulants such as long-acting methylphenidate (Concerta, Ritalin LA, Metadate), long-acting dexmethylphenidate (Focalin XR), extended release amphetamine (Adderall XR), and lisdexamfetamine (Vyvanse). Although often effective, there is a need for ongoing monitoring for continuous use of stimulant medications, as well as evidence poor medication adherence.

Some of the side effects of stimulants include poor appetite and sleep difficulties, and the rate occurrence of tics.

What about non-stimulant drugs for adult ADHD?

Dr. Adler: It's important to recognize that some ADHD patients fail to respond to stimulants or have side effects as noted before (tics, severe loss of appetite, marked insomnia).[7] For these patients, the non-stimulant drug atomoxetine (Strattera®) has been used. Atomoxetine is a selective inhibitor of the presynaptic norepinephrine transporter that increases norepinephrine and dopamine levels, especially in the prefrontal cortex. Atomoxetine is the only non-stimulant drug currently approved for adult ADHD. Its mechanism of action suggests that atomoxetine is unlikely to have abuse potential or to cause motor tics, but atomoxetine has a slower onset of action than do stimulants. Atomoxetine has a longer duration of action than the stimulants with the possibility of symptom relief during the evening and early-morning hours. However, atomoxetine has a boxed warning regarding the increased risk of suicidal ideation in children and adolescents, and a warning regarding severe liver injury.

The other non-stimulants, clonidine ER and guanfacine ER, are only approved for children and adolescents and are contraindicated in patients with a history of hypersensitivity to products containing those ingredients. In addition, the side effects of clonidine and guanfacine include dose-dependent hypotension and bradycardia, as well as somnolence and sedation.

What about alternative medicine for adult ADHD?

Dr. Adler: Many ADHD patients are given a variety of unproven treatments and there are many claims about clinical benefits. However, complementary and alternative treatments (CATs) should only be used if beneficial effects can be empirically demonstrated. In general, recently there has been increasing research on CATs for pediatric and adult ADHD. However, none of these treatments currently meet criteria as acceptable complementary or alternative treatments based on comparative, controlled clinical studies. More research needs to be done in this area that will include more double blind, placebo controlled trials in reliably diagnosed patients with ADHD.

Are there long-term consequences of untreated ADHD?

Dr. Adler: Many ADHD adults were not diagnosed with ADHD in childhood because the minimal demands of childhood and the protective structure of their environments may have masked the behavioral or function impact of their symptoms.[1] These same individuals have much greater impairment with the emerging academic, occupational, and social demands of adulthood.

The costs due to untreated adult ADHD are enormous and result in higher rates of academic underachievement, unemployment, underemployment, divorce, marital separation, substance abuse, cigarette smoking, and motor vehicle accidents.[4,5]

Many adults with ADHD are often living below their potential because of low self-esteem and lack of motivation related to the persistence their symptoms. It is likely that better recognition and earlier treatment intervention will markedly improve their performance and quality of life.

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